AUTHOR: Meyaard Linde; Hovenkamp Egbert; Pakker Nadine; Van Der Pouw Kraan Tineke C T M; Miedema Frank(a)
AUTHOR ADDRESS: (a)Dep. Clin. Viro-Immunol., Central Lab. Netherlands Red Cross Blood Transfusion Serv., Plesmanlaa, Netherlands

JOURNAL: Blood 89 (2):p570-576 1997
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The role of interleukin-12 (**IL-12**) in Th1 cell differentiation is well established. The heterodimer p70, composed of a p40 and a p35 chain, is the biologically active form. **IL-12** production by human monocytes is enhanced by interferon-gamma (IFN-gamma) and inhibited by IL-10 and prostaglandin E-2 (PGE-2). Peripheral blood mononuclear cells from human immunodeficiency virus (HIV)-infected individuals reportedly have impaired **IL-12** p40 and p70 production on stimulation with Staphylococcus aureus Cowan I (SAC) in vitro. Both PGE-2 and IL-10 previously were proposed to be instrumental in this defect in **IL-12** production. Here, we studied **IL -12** p40 and p70 production in relation to IL-10 and PGE-2 production in whole blood cultures from HIV-infected individuals. On stimulation with lipopolysaccharide, **IL-12** production was normal. However, on stimulation with SAC, **IL-12** p40 and p70 production was decreased in HIV-infected individuals and correlated significantly with decreased peripheral blood CD4+ T-cell number and T-cell reactivity to CD3 **monoclonal antibody** in vitro. However, IL-10 and PGE-2 production in cultures from HIV-infected individuals was normal and did not relate to **IL-12** production. In conclusion, **IL-12** production by cells from HIV-infected individuals is impaired under certain conditions in vitro

3-10-99
Search

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? s monoclonal(w)antibod?

          408393  MONOCLONAL
         1284882  ANTIBOD?
      S3  336837  MONOCLONAL(W)ANTIBOD?
? s S3 and IL-12

          336837  S3
             234  IL-12
      S4       6  S3 AND IL-12
? s S4 and IL(w)12

               6  S4
          195994  IL
         1169949  12
            7117  IL(W)12
      S5       6  S4 AND IL(W)12
? T S5/7/all


 5/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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11522333   BIOSIS NO.: 199800303665
Peritransplant tolerance induction with anti-CD3-immunotoxin: A matter of
  proinflammatory cytokine control.

AUTHOR: Contreras Juan L; Wang Pei X; Eckhoff Devin E; Lobashevsky Andrew L
  ; Asiedu Clement; Frenette Luc; Robbin Michelle L; Hubbard William J;
  Cartner Samuel; Nadler Steven; Cook William J; Sharff Joshua; Shiloach
  Joseph; Thomas Francis T; Neville David M Jr; Thomas Judith M
AUTHOR ADDRESS:  UAB Transplant Cent., Boshell Diabetes Build. 802, 1808
  7th Street South, Birmingham, AL 35294-0012, USA

JOURNAL: Transplantation (Baltimore)  65 (9):p1159-1169 May 15, 1998
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background. Tolerance is gaining momentum as an approach to
  reduce lifelong immunosuppressive therapy while improving transplant
  longevity. Anti-CD3 immunotoxin (IT), FN18-CRM9, has potential to induce
  tolerance owing to its exceptional ability to deplete sessile lymph node
  T cells. However, if initiated at the time of transplantation,
  alpha-CD3-IT alone elicits a proinflammatory cytokine response,
  precluding establishment of tolerance. Methods. Four groups of rhesus
  monkeys received kidney allografts and immunosuppression. Three groups
  received alpha-CD3-IT alone or alpha-CD3-IT supplemented with
  15-deoxyspergualin (DSG) and/or methylprednisolone (MP). One group
  received alpha-CD3-monoclonal antibody with DSG and MP.
  Cytokines were measured by enzyme-linked immunosorbent assay. Results:
  Supplementing peritransplant alpha-CD3-IT treatment with a brief course
  of DSG and MP promoted rejection-kidney allograft acceptance in 75% of
  macaques followed for up to 550 days. Among those given alpha-CD3-IT
  alone or with MP, none were long-term survivors. Tolerance developed
  after alphaCD3- IT, DSG, and MP treatment, but not when the unconjugated
  alpha-CD3 monoclonal antibody was substituted for IT.
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Systemic production of proinflammatory cytokines interferon-gamma (IFN-gamma) and tumor necrosis factor-alpha induced after peritransplant alpha-CD3-IT was prevented only in animals given DSG. Despite high levels of interleukin (**IL**)-**12** in the first month after transplant, tolerant recipients exhibited **IL-12** resistance, as evidenced by baseline plasma levels of IFN-gamma but elevated HA. DSG was shown to inhibit **IL-12**-driven IFN-gamma production by a mechanism associated with inhibition of nuclear factor kappa-B. Conclusions. In this model, peritransplant induction of tolerance is promoted by efficient elimination of sessile lymph node T cells and control of the proinflammatory IFN-gamma response by a mechanism that appears to involve resistance to **IL-12**.

5/7/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11217412 BIOSIS NO.: 199799838557
Active specific immunotherapy with mouse anti-idiotypic (anti-id) mAb MK2-23.

AUTHOR: Ferrone S; Desai S; Wang X; Zhang D; Noronha E; Kymisses A
AUTHOR ADDRESS: New York Med. Coll., Dep. Microbiol. Immunol., Basic Sci. Build., Room 308, Valhalla, NY 10595, USA

JOURNAL: International Journal of Oncology 11 (SUPPL.):p932 1997

CONFERENCE/MEETING: 2nd World Congress on Advances in Oncology Athens, Greece October 16-18, 1997
ISSN: 1019-6439
RECORD TYPE: Citation
LANGUAGE: English

5/7/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11165990 BIOSIS NO.: 199799787135
Autoantibody production and cytokine profiles of MHC class I (beta-2-microglobulin) gene deleted New Zealand Black (NZB) mice.

AUTHOR: Chen Shao-Yuan; Takeoka Yuichi; Pike-Nobile Larry; Ansari Aftab A; Boyd Richard; Gershwin M Eric(a)
AUTHOR ADDRESS: (a)Div. Rheumatol., Allergy and Clin. Immunol., Sch. Med., Univ. Calif. at Davis, Davis, CA 95616, USA

JOURNAL: Clinical Immunology and Immunopathology 84 (3):p318-327 1997
ISSN: 0090-1229
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We established a colony of MHC class I deleted (knockout) NZB mice, which lack the beta-2 microglobulin gene (NZB.beta-2m-/-), to characterize the contribution of MHC class I to the thymic microenvironment abnormalities, autoantibody production and lupus-like disease of NZB mice. Using an extensive panel of well characterized **monoclonal antibodies** defining thymic epithelial and other stromal elements, we demonstrated that deletion of MHC class I molecules does not change the thymic abnormalities, including the presence of a cortical epithelial cell free region, ectopic expression of medullary epithelial antigens, and the irregular shape of the medullary epithelial network of NZB mice. Moreover, the decreased staining of MTS 33+ cells, a marker of premature thymocyte maturation, was also seen in

NZB.beta-2m-/-. However, although NZB cntdot beta-2m-/- mice had approximately the same levels of IgM and IgG anti-ss and dsDNA antibodies when compared to control NZB mice, there were significant alterations in the incidence and onset of anti-erythrocyte antibody levels. NZB.beta-2m-/- had a lower incidence and a delayed onset of anti-erythrocyte autoantibody production compared to that seen in NZB mice. We also compared constitutive and PHA-P-driven levels of IFN-gamma, IL-4, IL-6, and **IL-12** in cells from NZB, NZB.beta-2-/-, and control C57BL/6 mice. Mitogen stimulated cells showed a decreased IFN-gamma, and a marked increase in IL-6 and **IL-12** in NZB and NZB.beta-2m-/- mice.

5/7/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11047884 BIOSIS NO.: 199799669029
Modulation of the expression of membrane-bound regulators of complement activation on renal tumor cell lines by cytokines.

AUTHOR: Gorter A(a); Blok V T(a); Tijsma O(a); Daha M R; Fleuren G J(a)
AUTHOR ADDRESS: (a)Dep. Pathol., Leiden Univ. Hosp., Leiden, Netherlands

JOURNAL: Experimental and Clinical Immunogenetics 14 (1):p92 1997

CONFERENCE/MEETING: 6th European Meeting on Complement in Human Disease Innsbruck, Austria March 12-15, 1997
ISSN: 0254-9670
RECORD TYPE: Citation
LANGUAGE: English

5/7/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10823461 BIOSIS NO.: 199799444606
Regulation of **IL-12** enhanced NK cytotoxicity by **monoclonal antibody** against ICAM-1 molecules in NK cells.

AUTHOR: Cho D H(a); Song H K(a); Kang H S(a); Yoon S R(a); Lee H G(a); Pyun K H(a); Lee W J; Rothlein R; Kim Y B; Choi I(a)
AUTHOR ADDRESS: (a)KRIBB, Taejon, South Korea

JOURNAL: Journal of Allergy and Clinical Immunology 99 (1 PART 2):pS465 1997

CONFERENCE/MEETING: Joint Meeting of the American Academy of Allergy, Asthma and Immunology, the American Association of Immunologists and the Clinical Immunology Society San Francisco, California, USA February 21-26, 1997
ISSN: 0091-6749
RECORD TYPE: Citation
LANGUAGE: English

5/7/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10759886 BIOSIS NO.: 199799381031
Interleukin-12 (**IL-12**) production in whole blood cultures from human immunodeficiency virus-infected individuals studies in relation to IL-10 and prostaglandin E-2 production.

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   6.  DIALOG(R) Document Delivery
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      S2        0   PRESKY, DAVID
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Custer, Tara

From: Custer, Tara
Sent: Friday, February 12, 1999 2:52 PM
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Subject: Case ~~09/174,656~~ 09/232,512

Please send the following articles to my mailbox ASAP:

1. Clin. Immunol. and Immunopathol. 84 (3): p 318-327 1997
2. J. of Allergy and Clin. Immunology 99; (1 part 2); pS465
3. Blood 89: (2): p570-576 1997

Thanks

Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
CM1 9D04
Mail Room 9OC1

Custer, Tara
From: Custer, Tara
Sent: Monday, March 1, 1999
To: STIC-Biotech/ChemLib
Subject: 09/232,522

TEXT SEARCH

Please search the attached claims (1-33 only), along with search of inventors (on biblio sheet) and return results along with copy of claims to my mailbox. A copy of the claims is enclosed. Thanks.

The invention and some key words/search terms are listed:

1. A monoclonal humanized antibody to the human IL-12 p75 heterodimer which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer wherein the monoclonal antibody
   a. Reacts w/an eptiope presented by the p75 heterodimer of human IL-12 but is not reactive with any epitope presented by said p40 subunit
   b. Is produced from a cell line of the mouse which is deficient in the gene encoding said p35 subunit or the p40 subunit of IL-12
   c. Cross reacts w/ the rhesus monkey IL-12
   d. Produced by a hybridoma having ATCC # HB-12446, 12447, 12448, or 12449
   e. Neutralizes 90% fo the bioactivity of human IL-12 by inhibiting IL-12 stimulated PHA-activated human lymphoblast proliferation (IFN-gamma production) wherein the concentration of the antibody is 0.5 ug/mL and the concentration of human IL-12 is 0.25 ng/mL

2. A hybridoma capable of producing the monoclonal antibody mentioned above

S (IL-12 or cytotoxic(w)lymphocyte(w)maturation(w)factor or NK(w)CSF or natural(w)killer(w)cell(w)stimulatory(w)factor or heterodimeric(w)cytokine? Or NK(w)LAK or
S L1 and (p35? And p40?) or (35 kDa and 40kDa) and (p75? Or 75kDa) or epitope? or subunit?
S L2 and (monoclonal(w)antibod? Or antagonist? Or heterodimeric(w)specific(w)antibod? Or 16F2 or 16G2 or 20E11 or 5F2 or 20C2) → or 5F2, 16F2, 16G2, 20E11, [illegible], 20C2,
S L2 and (humaniz?)
S L3 and cell(w)line? And (mouse? Or mammal? Or knock(w)out) → or SP2/0 or NS/0
S L4 and (monkey? ~~Or rhesus?~~)
S L5 and (hybridoma? Or HB12447) or ATCC?
S L6 and (neutraliz? Or deplet? Or destroy? Or decreas? Or downregulat?) or inhibit or block
S L7 and (PHA? Or phytohemoagglutinin?) human(w) lymphoblast or lymphoblast?
S L8 and IFN?
S L9 and (lymphoblast?(w)proliferation?)
S L10 and (concentration? Or .25(w)ng(w)mL or .5(w)ug(w)mL)
S L11 and (deficient? Or lack? Or mutat?)(p)(p35? And p40?)
S L12 and (immunoassay? Or ELISA? Or lymphocyte(w)proliferation(w)assay?) competitive(w) immunoassay or assay cross (blocking, binding assay?

rhesus ~~PBP~~ (w) monkey or rhesus and cross react

All relevant references can be printed

Thanks.
Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
Building CM1 Room 9D04

neutralize in vivo rhesus monkey activity

Custer, Tara

From: Custer, Tara
Sent: Thursday, March 04, 1999 9:23 AM
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1. Clin. Immunol. and Immunopathol. 84 (3): p 318-327 1997
2. J. of Allergy and Clin. Immunology 99; (1 part 2); pS465
3. Blood 89: (2): p570-576 1997

Thanks

Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
CM1 9D04
Mail Room 9OC1

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Subject: FW: 09/232,522

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1. Hybridoma; 1997 Aug.; 16(4); 363-9
2. J. of Immunol.; March 1998; 160(5); 2174-9
3. Ann. Review of Immunol.; 1998; 16; 495-521
4. Infection and Immunity; Nov. 1997; 65(11); 4734-7
5. Eur. Jounral of Immunol.; 1997; Jan.; 27 (1); 147-54
6. J. Allergy and Clinical immunology; 1997; Vol. 99; No. 1; part 2; p. S52
7. Proc. Natl. Acad Sci.; 1996; Nov. 26; 93(24); 14002-7
8. FASEB Journal; 1996; Vol. 10; No. 6; p. A1323
9. FASEB Journal; 1996; Vol. 10; No. 6; p. A1310
10. Annals of the NY Acad. of Sci. ; 1996; Oct 31; 795; 390-3
11. Eur. J. Immunol.; Feb. 1996; 26(2); 345-50
12. J. of Immunological Methods; Jan. 1996; 189(1); 15-24
13. Annals of NY Acad of Sciences; 1996 Oct. 795; 1-12
14. J. Biol. Chem.; 1995; (17); 270 (11); 5864-71
15. Research in Immunology; 1995 Sep-Oct.; 146; (7-8); 439-45
16. 9th International Congress of Immunol.; 1995; pp. 299; July 23-29
17. Eur. J. of Immunology; 1995; 25 (1); 200-6
18. FASEB Journal; 1994; Vol. 8; No. 4-5; p. A963;
19. J. Immunology; 1994; 153 (1); 128-36

Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
CM1 9D04
Mail Room 9OC1

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1. Proc. Natl. Acad. Sci.; Vol. 88; 4143
2. J. Immunol; 1991; 146; 3074
3. Arch. Biochem. Biophys. 294:230; 1992
4. J. Exp. Med.; 176: 1387: 1992
5. J. Immunol.; 154; 116; 1995
6. Eur. J. Immunol; 25:200; 1995
7. Cytokine; 6; 8A2a; 1994
8. Eur. J. Immunol.; 26:1553-59; 1996
9. Immunity; 4:471-481 (1996)

Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
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1. J. Immunol.; 147; 1548 (1991)

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Patent Examiner
Art Unit 1644
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1. J. Immunol.; 153; 128 (1994)

Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
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